

Molecular Characterization and Functional Exploration of Nuclear Receptors in hiPSCs

Grant Award Details

Molecular Characterization and Functional Exploration of Nuclear Receptors in hiPSCs

Grant Type: Basic Biology II

Grant Number: RB2-01530

Project Objective: To define how nuclear hormone receptors (NHR) contribute to the formation and behavior of adipose derived hiPSCs

Investigator:

Name:	Ronald Evans
Institution:	Salk Institute for Biological Studies
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: \$1,712,880

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Molecular Characterization and Functional Exploration of Nuclear Receptors in hiPSCs

Public Abstract:

Our lab is known for its discovery of the family of nuclear hormone receptors (NHRs) that use vitamins/hormones to control genes and thereby regulate embryonic development, cell growth, physiology and metabolism. Of 48 known NHRs, we discovered that a unique subset of 38 receptors are expressed in adipose-derived human induced pluripotent stem cells (hiPSCs). The process of converting adult cell types like skin or fat into stem cells literally occurs in the nucleus by a process known as epigenetic reprogramming. A unique property of NHRs that distinguishes them from other classes of receptors is their ability to directly interact with and control the expression of genomic DNA. Consequently, NHRs play key roles in both the etiology and the treatment of disease by controlling genes. Drugs targeting NHRs are among the most widely prescribed in the world. While adipose-derived iPSCs express 38 NHRs, virtually nothing is known about their function in controlling stem cell renewal and differentiation into specific cell types (cell fate). How the extensive family of hormonal ligands can be used to control iPSC generation, maintenance and cell fate has profound implications for regenerative medicine. We wish to take advantage of our lab's expertise to understand, at the molecular and hormonal level, how nuclear receptors can be exploited to accelerate the use of iPSCs in regenerative medicine.

Statement of Benefit to California:

Our lab is known for its discovery of the family of nuclear hormone receptors (NHRs) that use hormones to control genes and thereby regulate embryonic development, cell growth, physiology and metabolism. This work was all done in California and has brought in more than \$100,000,000 of private and federal funding to my group over the last 30 years. It has led to my employment of 150+ people and the publication of more than 300 research papers. Three biotech companies were founded from this work that in aggregate raised more than \$1B in research and development support. Several FDA approved drugs for cancer, diabetes, osteoporosis and low white blood cells (leukopenia) were developed with this technology.

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